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Analysis of Influence of Catecholamine and Tachycardia during Supine Exercise in Patients with Mitral Stenosis and Sinus Rhythm

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The haemodynamic effects of exercise consist of integrated effects of tachycardia, catecholamine stimulation, and Frank-Starling mechanism (Sonnenblick *et al.*, 1965; Epstein *et al.*, 1965; Braunwald *et al.*, 1967). In patients with mitral stenosis, filling of the left ventricle, and, consequently, cardiac output, is very dependent on the diastolic filling period; hence, tachycardia by decreasing this interval may impinge on ventricular filling, with an increase in the mitral valve gradient. In addition, the increase in flow due to the inotropic effect of catecholamine stimulation in the presence of a relatively fixed and stenosed valve can increase the mitral valve gradient (Whalen *et al.*, 1963). To elucidate the relative role of the above-mentioned factors, i.e. tachycardia and catecholamine stimulation, haemodynamic studies were performed in patients with mitral stenosis at rest and during supine exercise, at control state and after beta blockade, during spontaneous and controlled heart rates. The results of this study indicate that after elimination of the catecholamine influence the heart rate and cardiac output diminish, and hence mitral valve gradient decreases. When the heart rate was controlled during beta blockade, the mitral valve gradient increased, mainly because of a reduction in the diastolic filling period.

Subjects and Methods

Cardiac haemodynamic studies were performed in a post-absorptive state in 7 patients with pure mitral stenosis and sinus rhythm. Pre-medication consisted of diphenhydramine hydrochloride 50 mg., and pentobarbitone sodium 75 mg., intramuscularly. A No. 6F NIH catheter was inserted into the right antecubital vein and was positioned in the main pulmonary artery. Pressures in the right atrium, right ventricle, and pulmonary artery were recorded by this catheter. A unipolar electrode catheter* was inserted into the same vein and its tip was positioned in the right atrium. Electrical pacing of the heart was performed at threshold stimulus using a Medtronic Generator, model 5800. A No. 18-T Cournand needle was inserted percutaneously into the right brachial artery. Transseptal left heart catheterization (Brockenbrough, Braunwald, and Ross, 1962) was performed and the Brockenbrough catheter was positioned in the left atrium. The left ventricle was entered using a polyethylene catheter (PE-50) which was advanced through the Brockenbrough catheter into the left ventricle. Cardiac output was measured by the direct Fick principle. Simultaneous left ventricular-left atrial, left atrial-pulmonary arterial, and left ventricular-brachial arterial pressures were recorded by Statham transducers, model 23Db. The systolic ejection time was determined from the brachial artery pressure. The mean systolic ejection rate was determined by dividing stroke index (ml./m.^{2}) by the duration of systolic ejection time in seconds. Mean pressures were determined by electrical integration. The mitral valve area was calculated by planimetric integration of left ventricular-left atrial diastolic pressure gradient and the use of Gorlin's hydraulic formula for the stenosed valve (Gorlin and Gorlin, 1951). Pulmonary arteriolar resistance was calculated by the formula:

$$\frac{\text{Mean pulmonary arterial pressure} - \text{mean left atrial pressure (mm. Hg)}}{\text{Cardiac output (l./min.)}} \times 80.$$

The undamped natural frequency and damping ratio for the Brockenbrough catheter-manometer system were 125 cycles/sec. and 0·556, respectively. Identical values for the polyethylene catheter-manometer system were

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* U.S. Catheter and Instrument Corp., Catalog No. 5651.

TABLE

HAEMODYNAMIC DATA IN 7 PATIENTS WITH MITRAL STENOSIS

Case No.		Sex and age	BSA ($m.^2$)	O_2 consumption ($cm.^3/m.^2$)	Heart rate /min.	Cardiac index (l./min./$m.^2$)	AV O_2 diff. (vol. %)	Stroke index (ml./beat/$m.^2$)	Pressures: Brachial artery Syst.	Pressures: Brachial artery Diast.	Pressures: Brachial artery Mean	Pressures: Left ventr. Syst.	Pressures: Left atr. Diast.
1	C-R	F34	1·77	133	113	2·52	5·3	22·3	138	78	(90)	128	−2 (32)
	C-Ex			220	120	2·88	7·7	24·1	143	70	(97)	132	−5 (33)
	R-Bl			133	86	1·99	7·6	23·2	132	72	(88)	120	1 (19)
	Ex-Bl			180	98	1·67	6·7	17·0	125	70	(95)	123	3 (21)
	R-Bl-P			—	119	—	10·8	—	126	75	(97)	112	−1 (27)
	Ex-Bl-P			208	119	2·26	9·2	19·0	125	75	(88)	112	0 (25)
2	C-R	M50	2·0	105	77	2·90	3·6	37·6	122	62	(85)	108	1 (20)
	C-Ex			295	102	4·46	6·6	43·7	160	72	(100)	130	0 (38)
	R-Bl			106	67	2·70	3·9	40·3	135	75	(95)	128	6 (23)
	Ex-Bl			266	85	2·99	8·9	35·2	150	80	(115)	130	6 (38)
	R-Bl-P			110	67	2·19	5·0	32·7	140	75	(102)	130	7 (25)
	Ex-Bl-P			324	109	3·44	9·4	31·6	165	85	(110)	140	1 (35)
3	C-R	F54	1·65	101	90	2·89	3·5	32·1	118	52	(75)	105	6 (27)
	C-Ex			204	106	3·71	5·5	35·0	150	60	(85)	145	1 (42)
	R-Bl			96	67	2·40	4·0	35·8	110	50	(75)	108	11 (20)
	Ex-Bl			207	85	2·91	7·1	34·3	125	58	(80)	116	16 (38)
	R-Bl-P			105	90	2·83	3·7	31·4	108	55	(75)	100	8 (21)
	Ex-Bl-P			354	110	3·77	9·4	34·3	140	65	(88)	128	4 (40)
4	C-R	F31	1·45	95	83	1·91	4·9	33·4	120	60	(78)	92	5 (22)
	C-Ex			280	107	2·47	11·3	25·0	130	65	(75)	98	6 (35)
	R-Bl			103	62	1·80	5·7	29·0	103	55	(75)	90	10 (17)
	Ex-Bl			230	80	1·70	13·5	21·3	100	50	(65)	78	10 (25)
	R-Bl-P			109	90	2·13	5·1	34·4	120	65	(85)	98	4 (25)
	Ex-Bl-P			251	105	1·97	12·7	18·7	108	58	(75)	90	7 (34)
5	C-R	F50	1·51	126	81	3·32	3·8	41·0	147	74	(105)	135	10 (14)
	C-Ex			281	125	4·25	6·6	34·0	174	87	(113)	150	3 (26)
	R-Bl			115	66	2·87	4·0	43·5	151	74	(100)	138	9 (10)
	Ex-Bl			287	86	3·59	8·0	41·7	171	80	(114)	153	10 (19)
	R-Bl-P			125	79	3·30	3·8	41·8	157	71	(106)	141	9 (10)
	Ex-Bl-P			276	117	3·45	8·0	29·5	158	81	(105)	135	5 (17)
6	C-R	F42	1·63	132	83	2·57	5·2	31·0	106	54	(71)	95	1 (12)
	C-Ex			214	95	2·09	10·2	22·0	122	60	(81)	99	1 (19)
	R-Bl			107	77	1·69	6·3	22·0	105	60	(75)	87	0 (9)
	Ex-Bl			270	85	2·67	10·1	31·4	108	55	(75)	92	1 (15)
	R-Bl-P			123	81	2·04	6·0	25·2	112	62	(78)	90	1 (14)
	Ex-Bl-P			234	97	2·39	9·8	24·6	110	62	(80)	97	4 (19)
7	C-R	M34	2·10	117	80	2·80	4·2	35·0	141	80	(104)	133	6 (23)
	C-Ex			261	104	3·58	7·3	34·4	147	77	(100)	135	5 (30)
	R-Bl			110	82	2·09	5·3	25·5	152	95	(117)	140	6 (18)
	Ex-Bl			310	94	2·90	10·7	30·8	150	85	(115)	133	3 (27)
	R-Bl-P			112	82	2·44	4·6	29·8	150	90	(110)	133	8 (20)
	Ex-Bl-P			301	105	2·82	10·5	28·1	150	90	(120)	135	2 (27)
Mean values	C-R			116	86·7	2·70	4·4	33·2	127	66	(87)	114	4 (21)
	C-Ex			251	108	3·35	7·9	31·2	147	70	(93)	127	2 (32)
	R-Bl			110	72	2·22	5·3	31·3	127	69	(89)	116	6 (16)
	Ex-Bl			250	88	2·63	9·3	30·2	133	68	(94)	118	7 (26)
	R-Bl-P			114	87	2·49	5·6	32·5	130	70	(93)	115	5 (20)
	Ex-Bl-P			278	109	2·87	9·8	26·5	137	74	(95)	120	3 (28)

C-R: Control rest. C-Ex: Control exercise. R-Bl: Rest-beta blockade. Ex-Bl: Exercise-beta blockade. R-Bl-P: Rest-beta blockade-
Note: Mean values are given in parentheses.

125 cycles/sec. and 0·566. The above systems were tested with the polyethylene catheter inside the Brockenbrough catheter, hence simulating the simultaneous left ventricular-left atrial recording.

All recordings were made on an Electronics for Medicine Photographic Recorder, model DR-7, at a paper speed of 25 and 75 mm./sec. After obtaining control data at rest, exercise was performed in the supine position on a bicycle ergometer pedalled at 60 revolutions/min. at a load that the patient could tolerate for 6 minutes without extreme fatigue. Cardiac output and pressures were determined between the third and fifth minute of exercise when the heart rate and pressure were stable. After completion of exercise studies the patients rested for 10 to 15 minutes. At the end of this period, and after stabilization of various haemodynamic parameters, propranolol*, 0·1 mg./kg., was administered intravenously during a five-minute period. Cardiac output and pressures at rest and exercise were then obtained during spontaneous and controlled heart rates. This was accomplished in 2 consecutive but randomized runs. The exercise load and the temporal relation to

* Kindly supplied by Dr. Alex Sahagian-Edwards of Ayerst Laboratories.

AND SINUS RHYTHM DURING REST AND SUPINE EXERCISE

(mm. Hg)							Mitral diast. filling period (sec./min.)	Mitral valve diast. flow (ml./diast. sec.)	Resistance (dynes. sec. cm.$^{-5}$)			Mean syst. ejection rate (ml./sec.)	Mitral valve area (cm.^{2})
Mitral valve diast. grad.	Pulm. art.			Rt. atrium mean	Rt. ventr.				Total pulm.	Pulm. arteriol.	Total syst.		
	Syst.	Diast.	Mean		Syst.	Diast.							
27	110	45	(72)	(3)	105	0	30·4	147	1290	720	1610	88.2	0·91
27	118	48	(75)				31·2	164	1170	658	1520	102	1·02
16	92	48	(65)				30·6	115	1475	1040	2240	87·8	0·93
15	100	55	(70)				31·6	93·5	1900	1330	2580	73	0·78
20	102	47	(70)				27·4	—	—	—	—	—	—
24	105	52	(70)				27·4	146	1400	900	1760	83·2	0·96
17	49	22	(33)	(5)	35	7	35·0	166	455	180	1170	115	1·30
26	80	34	(60)				30·8	289	538	197	900	149	1·83
16	57	24	(37)				33·4	162	548	207	1400	123	1·31
22	75	35	(55)				32·5	184	735	227	1540	121	1·26
15	58	24	(41)				32·0	137	750	292	1860	101	1·14
31	80	40	(60)				28·7	239	695	292	1280	109	1·39
21	55	29	(36)	(3)	46	1	32·2	148	605	151	1250	100	1·04
26	62	39	(53)				29·2	210	692	143	1110	127	1·33
10	40	22	(28)				39·6	100	565	161	1510	100	1·02
18	58	33	(45)				32·6	147	750	116	1330	98	1·12
14	44	24	(30)				30·1	155	512	153	1280	102	1·34
27	73	33	(53)				30·2	206	680	167	1130	116	1·28
16	36	20	(27)	(6)	39	7	34·6	80	780	145	2250	114	0·65
23	63	34	(44)				33·2	108	980	200	1670	98	0·73
10	30	16	(20)				35·4	74	615	92	2300	88	0·75
12	43	23	(31)				38·8	63·6	1000	195	2100	70	0·60
17	39	23	(30)				29·6	104	775	130	2200	116	0·81
20	55	33	(41)				30·7	93·5	1140	195	2090	71	0·68
6·7	30	13	(20)	(4)	30	3	24·3	207	320	96	1670	121	2·6
14·4	47	24	(35)				20·8	309	435	112	1410	121	2·6
4·2	28	8	(17)				28·8	150	313	129	1850	122	2·4
8·6	41	16	(29)				22·2	244	429	148	1680	116	2·6
7·3	29	12	(19)				22·4	222	305	145	1700	120	2·6
10·5	36	19	(27)				20·2	258	415	153	1605	101	2·5
14	32	17	(25)	(2)	32	0	33·4	128	477	210	1350	119	1·1
18	47	23	(35)				34·6	99	820	375	1890	85	0·9
10	24	15	(17)				33·0	84	492	232	2180	87·5	0·86
15	30	17	(25)				32·6	134	460	183	1370	124	1·11
16	37	21	(28)				33·6	99	672	336	1870	94	0·80
17	36	20	(28)				31·0	126	595	206	1640	96	0·98
18	60	23	(41)	(4)	60	6	26·2	225	557	245	1415	121	1·72
19	66	29	(49)				34·0	221	522	202	1060	127	1·64
13	42	23	(30)				28·4	155	547	219	2130	86	1·38
20	62	33	(46)				28·9	210	605	250	1510	101	1·51
15	49	27	(34)				28·8	178	530	218	1715	100	1·48
20	70	30	(45)				28·1	212	606	242	1615	106	1·52
17·1	53	24	(36)	—	—		30·9	157	640	250	1531	111	
22·0	69	33	(50)				30·5	200	736	270	1365	115	
11·3	45	22	(30)				32·7	120	651	297	1944	99	
15·8	58	30	(43)				31·3	154	840	350	1730	100	
15·0	51	25	(36)				29·1	149	590	212	1771	105	
21·3	65	32	(46)				28·0	183	790	308	1588	97	

pacing. Ex-Bl-P: Exercise-beta blockade-pacing.

obtain various haemodynamic parameters were identical to those of the control state. The data were subjected to statistical analysis for small samples using Student's t test for paired samples (Snedecor, 1956).

Results

Haemodynamic data are shown in the Table. For ease of demonstration, the data are tabulated in orderly sequence; however, during the actual beta blockade study the heart rate was controlled at random.

Cardiac Index (l./min./m.²) (Fig. 1). The mean cardiac index at control resting state was 2·70 l./min./m.^{2} and increased to 3·35 l./min./m.^{2} during exercise. During rest-beta blockade, the mean cardiac index was 2·22 l./min./m.^{2}, which was significantly lower than the control resting cardiac index ($p < 0·005$); and increased to 2·63 l./min./m.^{2} during exercise ($p < 0·025$ when compared to control exercise). During rest-beta blockade-pacing state, cardiac index was 2·49 l./min./m.^{2}, which was not statistically different from the control cardiac

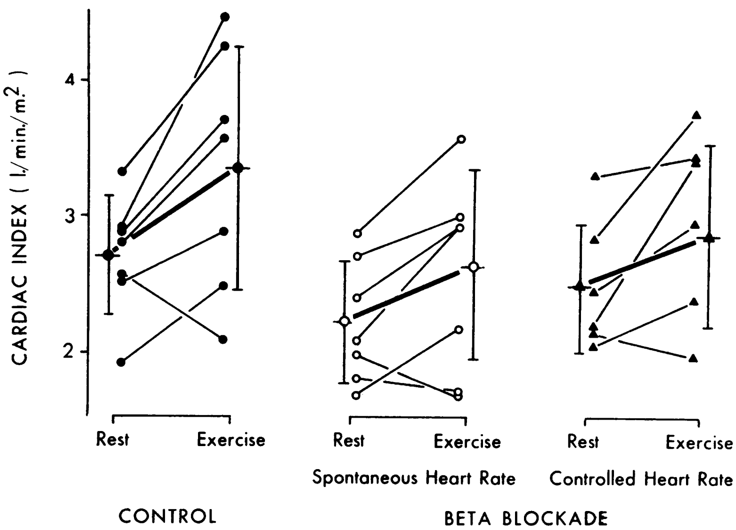

FIG. 1.—Cardiac index (l./min./m.^{2}) during control state (rest and exercise) and after beta blockade during spontaneous and controlled heart rate. Mean $\pm$SD are shown by horizontal bars.

index. During exercise-beta blockade-pacing, cardiac index increased to 2·87 l./min./m.^{2}, which was significantly lower than the control exercise cardiac index ($p < 0·05$).

Heart Rate. Mean heart rate at control resting state and exercise was 87 and 108/min, respectively. After beta blockade the heart rate was 72/min. at rest and increased to 88/min. during exercise. Heart rate during rest-beta blockade-pacing was 87/min., and during exercise-beta blockade-pacing was 109/min.

Stroke Index (ml./beat/m.^{2}). Mean stroke index during control-resting state was 33·2 ml./beat/m.^{2} and during exercise was 31·2 ml./beat. The changes in stroke index during beta blockade at rest and exercise, during spontaneous or controlled heart rate, were not statistically different from control rest and exercise values.

Arteriovenous Oxygen Difference (vol. %) (Fig. 2). Mean arteriovenous oxygen difference during control resting state was 4·4 vol. per cent and increased to 7·9 vol. per cent with exercise. During rest-beta blockade, arteriovenous oxygen difference was 5·3 vol. per cent ($p < 0·025$ as compared to control), and increased to 9·3 vol. per cent during exercise ($p > 0·05$). During rest-beta blockade-pacing, arteriovenous oxygen difference was 5·6 vol. per cent ($p > 0·1$ as compared to control state) and increased to 9·8 vol. per cent during exercise-beta blockade-pacing, which was statistically different from control-exercise value ($p < 0·025$).

Left Atrial Pressure (Fig. 3). Mean left atrial pressure during control resting state was 21 mm. Hg and increased to 32 mm. Hg during exercise. Mean left atrial pressure during rest-beta blockade was 16 mm. Hg, which was significantly lower than the control state ($p < 0·05$). Mean left atrial pressure increased to 26 mm. Hg during exercise, which was statistically different from the control exercise value ($p < 0·025$). Mean left atrial pressure during rest-beta blockade-pacing was 20 mm. Hg, which was not significantly different from the control, and increased to 28 mm. Hg during exercise ($p < 0·05$). Hence, the increase in left atrial pressure from rest to exercise before beta blockade was 11 mm. Hg, after beta blockade without heart rate control it was 10 mm. Hg, and when the heart rate was controlled it was 8 mm. Hg.

Mitral Valve Diastolic Pressure Gradient (Fig. 4). Mitral valve diastolic gradient during control-resting state was 17 mm. Hg and increased to 22 mm. Hg during exercise. Mitral valve gradient during rest-beta blockade was 11 mm. Hg, which was statistically different from the control ($p < 0·01$), and increased to 16 mm. Hg with exercise ($p < 0·025$ when compared to control-exercise state). Mitral valve gradient during rest-beta blockade-pacing was 15 mm. Hg and increased to 21 mm. Hg during exercise, with no statistical difference as compared to

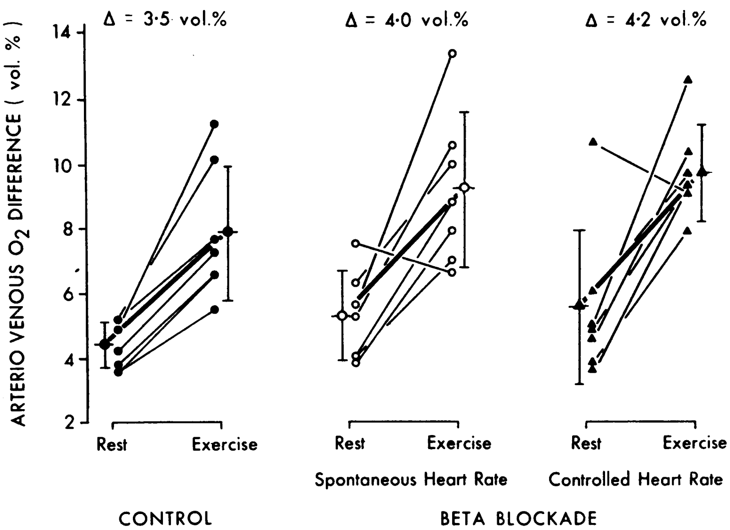

Fig. 2.—Arteriovenous oxygen difference at control state and after beta blockade during spontaneous and controlled heart rate. Mean ± SD are shown by horizontal bars.

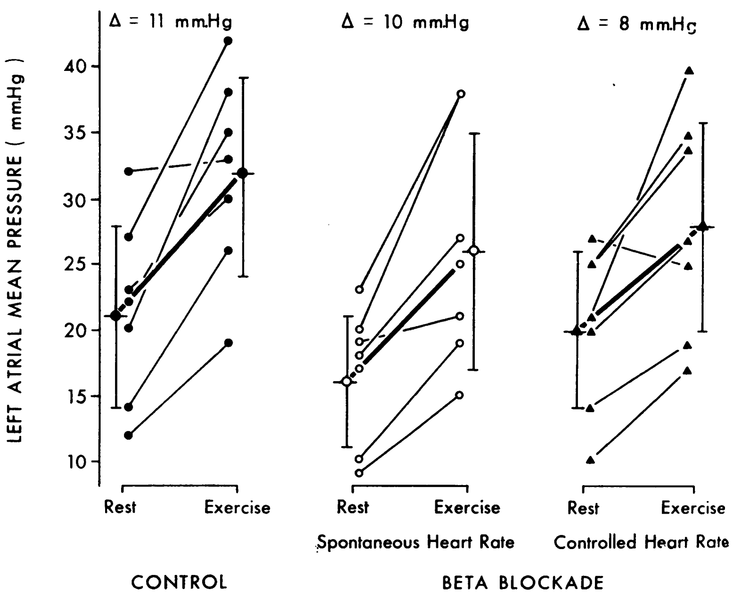

Fig. 3.—Left atrial mean pressure at control state and after beta blockade during spontaneous and controlled heart rate. Mean ± SD are shown by horizontal bars.

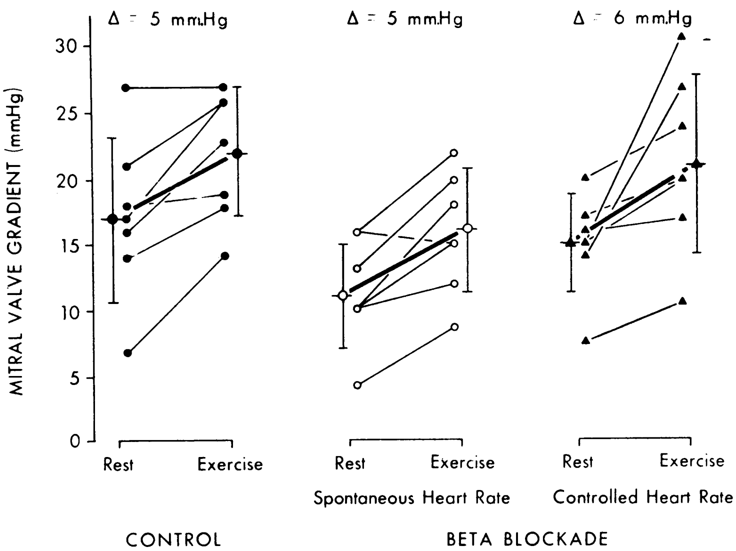

FIG. 4.—Mitral valve diastolic pressure gradient at control state and after beta blockade during spontaneous and controlled heart rate. Mean ± SD are shown by horizontal bars.

control. Hence, the increase in mitral valve gradient from rest to exercise before beta blockade was 5 mm. Hg, after beta blockade with spontaneous heart rate it was 5 mm. Hg, and with controlled heart rate it was 6 mm. Hg.

Mitral Diastolic Filling Period (sec./min.). Mean diastolic filling period during control resting state was 31 sec./min., with no change during exercise. During rest-beta blockade, the diastolic filling period was 33 sec./min. and during exercise-beta blockade it was 31 sec./min. Diastolic filling period during rest-beta blockade-pacing was 29 sec. and during exercise-beta blockade-pacing was 28 sec./min. Only the latter was statistically different from its respective control value ($p < 0{\cdot}05$).

Pulmonary Arterial Pressure. Mean pulmonary arterial pressure during control-resting state was 36 mm. Hg, with an increase to 50 mm. Hg during exercise. Mean pulmonary arterial pressure during rest-beta blockade was 30 mm. Hg ($p < 0{\cdot}025$ when compared to control resting state), with an increase to 43 mm. Hg during exercise ($p < 0{\cdot}005$ when compared to control exercise value). Mean pulmonary arterial pressure during rest-beta blockade-pacing was 36 mm. Hg with an increase to 46 mm. Hg during exercise ($p < 0{\cdot}025$ when compared to control exercise state). Hence, the increase in pulmonary artery pressure from rest to exercise before beta blockade was 14 mm. Hg. After beta blockade and during spontaneous heart rate it was 12 mm. Hg and when the heart rate was controlled it was 10 mm. Hg.

Pulmonary Arteriolar Resistance (dynes. sec. cm.$^{-5}$). Pulmonary arteriolar resistance during control resting state was 250 dynes. sec. cm.$^{-5}$, and with exercise was 270 dynes. sec. cm.$^{-5}$. The changes in pulmonary arteriolar resistance during beta blockade at rest and exercise during spontaneous and controlled heart rate were not statistically significant.

Left Ventricular Pressure. Left ventricular systolic pressure during control-resting state was 114 mm. Hg and during exercise it was 127 mm. Hg. The changes in left ventricular systolic pressure during beta blockade at rest and exercise with spontaneous or controlled heart rate were not statistically significant. Left ventricular end-diastolic pressure during control-resting state was 4 mm. Hg and decreased to 2 mm. Hg during exercise. Left ventricular end-diastolic pressure during rest-beta blockade was 6 mm. Hg; however, this was not statistically significant when compared to control ($p > 0{\cdot}05$). During exercise-beta blockade, mean left ventricular end-diastolic pressure was 7 mm. Hg, which was significantly higher than the control exercise value ($p < 0{\cdot}05$). Left ventricular end-diastolic pressure during rest-beta blockade-pacing and during exercise-beta blockade-pacing was 5 mm. Hg and 3 mm. Hg, respectively, with no statistically significant difference from control values.

Mean Systolic Ejection Rate (ml./sec./m.²). Mean systolic ejection rate during control-resting state was 111 ml./sec./m.² and was 115 ml./sec. during exercise. Mean systolic ejection rate during rest-beta blockade and exercise-beta blockade was 99·2 ml./sec. and 100 ml./sec., respectively, which were not statistically different from the control values. During rest-beta blockade-pacing, mean systolic ejection rate was 105 ml./sec. and during exercise-beta blockade-pacing it was 97 ml./sec. ($p < 0{\cdot}025$ as compared to control exercise).

Discussion

The results of this study indicate that beta-adrenergic blockade by propranolol diminishes cardiac output significantly and are in agreement with other reports (Chamberlain and Howard, 1964; Tsolakas, Davies, and Oram, 1965; Howitt, Tinker, and Wade, 1965; Cumming and Carr, 1966). The diminished flow and reduced heart rate after beta blockade caused diminution in mitral valve gradient and left atrial pressure. When the heart rate was controlled during exercise and beta blockade state, the diastolic filling period was significantly shorter than that of the control exercise. The shortening of the diastolic filling period during exercise-beta blockade-pacing as compared to the control-exercise is due to the fact that catecholamine stimulation during normal exercise increases the velocity of contraction with lengthening of the diastolic filling period; this effect is inhibited by beta blockade. Fig. 5 shows the relation between cardiac index, oxygen consumption, and arteriovenous oxygen difference during exercise. Cardiac output is highest during the control-exercise state when the influence of catecholamine and heart rate is present. There is no statistically significant difference in oxygen consumption between the control and the beta blockade study during spontaneous and controlled heart rates. Arteriovenous oxygen difference increased during beta blockade, with spontaneous and controlled heart rate indicative of a more complete oxygen extraction by tissues due to insufficient cardiac output.

Fig. 6 shows the relation between cardiac index and mitral valve gradient at rest and exercise. It is seen that, at rest and during beta blockade, cardiac index and mitral valve gradient decreased. When the heart rate was controlled, mitral valve gradient and cardiac index increased to levels similar to control values. Since cardiac index at rest and during beta blockade was significantly lower than control cardiac index ($p < 0{\cdot}005$), sympathetic influence must have existed in such patients. However, when the heart rate was controlled at rest and during beta blockade, the cardiac index was not significantly different from the control ($p > 0{\cdot}1$), indicating that the sympathetic tone at rest and in the supine position is minimal (Sonnenblick *et al.*, 1965; Glick and Braunwald, 1965) and can be compensated by simple tachycardia. During exercise-beta blockade-pacing, when the heart rate was kept constant at the level attained during the control exercise, the mitral valve gradient increased to the level of the control exercise, while the cardiac index was lower than the control cardiac index (Fig. 6). These data are consonant with our previous findings that tachycardia *per se* can significantly increase the mitral valve gradient with slight change in cardiac

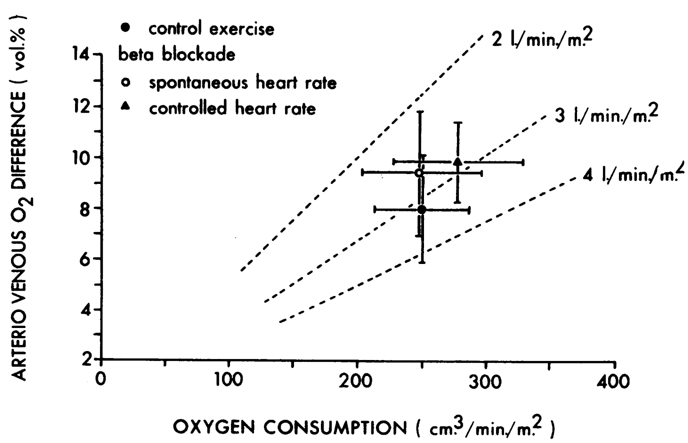

FIG. 5.—The relation between oxygen consumption (abcissa) and arteriovenous oxygen difference (ordinate) is shown. Cross bars indicate mean ±SD. Isobars indicate cardiac index (l./min./m.²).

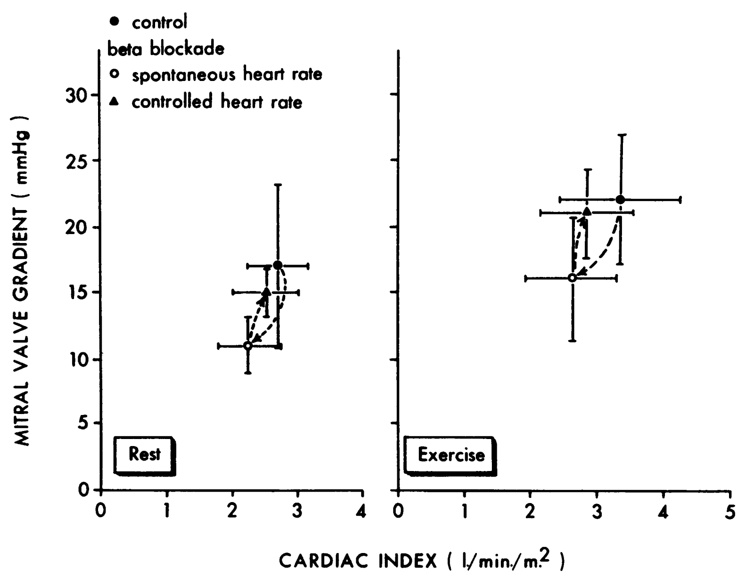

FIG. 6.—The relation between cardiac index (abcissa) and mitral valve gradient (ordinate) at rest and exercise is shown. Cross bars indicate mean ± SD.

output (Nakhjavan *et al.,* 1969). Studies by Sonnenblick and associates (1965), Epstein and associates (1965), and Braunwald and associates (1967) have indicated that the haemodynamic effects of exercise are integrated phenomena between tachycardia, catecholamine stimulation, and Frank-Starling mechanism, and that during submaximal exercise cardiac output can rise when one or more of these factors are blocked. The present study indicates that the role of catecholamine stimulation in patients with mitral stenosis without heart failure is of particular haemodynamic significance. The data obtained during exercise-beta blockade-pacing when compared to those of control exercise indicate that tachycardia of exercise, if not mediated by catecholamine stimulation, can only increase the mitral valve gradient and left atrial pressure without significant change in cardiac output. On the other hand, catecholamine influence during exercise, by its intense inotropic effect and increase in velocity of contraction, will abbreviate the systole, and, hence, the diastolic filling period is relatively longer during the initial exercise test when the catecholamine influence is intact. During exercise-beta blockade, left ventricular end-diastolic pressure increased significantly with a reduction in mean systolic ejection rate. During exercise-beta blockade-pacing, left ventricular end-diastolic pressure diminished and approached the control state, while mean systolic ejection rate remained low. The above-mentioned observations indicate that though the tachycardia of exercise influenced the left ventricular end-diastolic pressure due to a reduction in left ventricular volume, because of lack of catecholamine influence it did not increase the mean systolic ejection rate, and in fact this parameter was diminished.

In conclusion, it may be stated that when the chronotropic effects of beta blockade during exercise are eliminated by right atrial pacing, the mitral valve gradient increases disproportionately relative to cardiac output. The results indicate that the influence of catecholamine stimulation is of paramount significance in haemodynamic adjustments in patients with mitral stenosis.

SUMMARY

Seven patients with mitral stenosis and sinus rhythm were studied at rest and during supine exercise before and after beta-adrenergic blockade. After beta blockade, heart rate, cardiac output, and mitral valve gradient diminished. During exercise and beta blockade, when the heart rate was controlled and kept constant at the same level as that attained during control exercise, mitral valve gradient increased while cardiac output was lower than that during control exercise. The results indicate that the inotropic effects of catecholamine stimulation are of paramount significance in various haemodynamic changes noted during exercise.

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